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(54) Title: GAMMA-INTERFERON ACTIVITY MODULATING AGENT (54) Titre: AGENT MODULATEUR DE L'ACTIVITE DE L'INTERFERON-GAMMA (57) Abstract <p>The use of a modulating agent including a grouping of formula A-X-B for preparing a γ-interferon activity modulating drug is disclosed. In said formula, each of A and B is independently an oligosaccharide group with a sufficient anionic charge such that said oligosaccharide group has an affinity for a portion of the human γ-interferon C-terminal containing peptide sequence 125-131, and X is a spacer arm long enough to enable each of groups A and B to bind to one of said γ-interferon homodimer C-terminal peptide sequences. Said modulating agent is particularly useful for delaying the decomposition of γ-interferon, promoting the activation thereof and enabling it to have systemic and not just local activity. Said agent is also useful for modifying or inhibiting the local action of endogenous γ-interferon.</p> (57) Abrégé <p>Utilisation, dans la préparation d'un médicament modulateur de l'activité de l'interféron-γ, d'un agent modulateur comprenant un groupement de formule A-X-B, dans laquelle A et B représentent indépendamment un groupe oligosaccharidique portant une charge anionique suffisante pour conférer audit groupe oligosaccharidique une affinité pour une partie de l'extrémité C-terminale de l'interféron-γ humain contenant la séquence peptidique 125-131, et X est un bras espaceur de longueur suffisante pour permettre aux groupes A et B de se lier chacun à l'une desdites séquences peptidiques des extrémités C-terminales d'un homodimère d'interféron-γ. Cet agent modulateur permet notamment de retarder la dégradation de l'interféron-γ, de favoriser son activation, de permettre son action par voie générale et non simplement locale. Il permet également de modifier ou d'inhiber l'action locale de l'interféron-γ endogène.</p>			

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INTERNATIONAL SEARCH REPORT

International Application No

PC 96/01141

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FEBS LETT, LE11 MARS 1991, VOL. 280, NO. 1, PAGE(S) 152-4, XP002001351 LORTAT-JACOB H ET AL: "Interferon-gamma binds to heparan sulfate by a cluster of amino acids located in the C-terminal part of the molecule." cited in the application see abstract * paragraph Materials and methods * * paragraph Discussion * --- -/--	1-16

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>EUROPEAN JOURNAL OF IMMUNOLOGY, VOL. 25, NO. 3, PAGE(S) 688-692, March 1995, XP000568802 DAUEBENER W ET AL: "Heparin inhibits the antiparasitic and immune modulatory effects of human recombinant interferon-gamma" see abstract * paragraph discussion *</p>	1-16
Y	<p>C R ACAD SCI III, 1990, VOL. 311, NO. 4, PAGE(S) 143-7, FRANCE, XP002001352 LORTAT-JACOB H ET AL: "Matrice conjunctive et localisation d'un signal biologique: mise en evidence d'un recepteur matriciel pour l'interferon- gamma dans les membranes basale" cited in the application * paragraph Materials and methods * * paragraph Results /Discussion *</p>	1-16
Y	<p>BIOCHIM BIOPHYS ACTA, 15-9-1992, VOL. 1117, NO. 2, PAGE(S) 126-30, NL, XP000568807 LORTAT-JACOB H ET AL: "Binding of interferon-gamma to heparan sulfate is restricted to the heparin-like domains and involves carboxylic--but not N-sulfated--groups." cited in the application see abstract * paragraph Results *</p>	1-16
Y	<p>J CLIN INVEST, MARS 1991, VOL. 87, NO. 3, PAGE(S) 878-83, US, XP000568805 LORTAT-JACOB H ET AL: "High-affinity binding of interferon-gamma to a basement membrane complex (matrigel)." cited in the application see abstract * paragraph Results * * paragraph Discussion *</p>	1-16
P,X	<p>BIOCHEM J, SEP 1 1995, VOL. 310, NO. PT 2, PAGE(S) 497-505, ENGLAND, XP000568803 LORTAT-JACOB H ET AL: "Molecular organization of the interferon gamma-binding domain in heparan sulphate." see abstract * paragraph Results * see page 505, left-hand column</p>	1-16

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INTERNATIONAL SEARCH REPORT

 Inv. No. Application No
 PCT 96/01141

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATHOL., RES. PRACT., VOL. 190, NO. 9-10, PAGE(S) 920-2, 1994, XP000616388 LORTAT-JACOB, H. ET AL: "Interferon - gamma, an anti-fibrogenic cytokine which binds to heparan sulfate" see page 921, left-hand column ---	1-16
X	CELL. MOL. BIOL., VOL. 37, NO. 3, PAGE(S) 253-60, 1991, XP000616389 LORTAT-JACOB, H. ET AL: "Interferon - gamma C-terminal function: new working hypothesis. Heparan sulfate and heparin, new targets for IFN-gamma, protect, relax the cytokine and regulate its activity" cited in the application see page 257 ---	1-16
P,X	J. IMMUNOL., VOL. 157, NO. 2, PAGE(S) 864-873, 15 July 1996, XP002023901 LIAN, REBECCA H. ET AL: "IFN-gamma.-induced MHC class II gene expression is suppressed in endothelial cells by dextran sulfate" see abstract see figures ---	1-16
P,X	J. BIOL. CHEM., VOL. 271, NO. 27, PAGE(S) 16139-16143, 5 July 1996, XP002023902 LORTAT-JACOB, HUGUES ET AL: "Heparin decreases the blood clearance of interferon -. gamma. and increases its activity by limiting the processing of its carboxyl-terminal sequence" see paragraph Results ---	1-16
P,X	CLIN. EXP. IMMUNOL., VOL. 104, NO. 1, PAGE(S) 60-5, April 1996, XP000616393 RIX, D. A. ET AL: "Role of glycosaminoglycans (GAGs) in regulation of the immunogenicity of human vascular endothelial cells" see examples 4,5 ---	1-16

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INTERNATIONAL SEARCH REPORT

Int. Patent Application No.

PC 96/01141

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>CYTOKINE, VOL. 8, NO. 7, PAGE(S) 557-566, July 1996, XP000616381 LORTAT-JACOB, HUGUES ET AL: "Non-receptor-mediated tissue localization of human interferon - . gamma.: role of heparan sulfate /heparin-like molecules" see abstract see paragraph Discussion -----</p>	1-16

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